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POSTER ABSTRACTS

732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Dynamic Changes in Pre- and 3 Months Post-Transplant NGS MRD Status May Predict the Allogeneic Stem Cell Transplant Outcome of Patients with AML

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Introduction: To deal with the high propensity for relapse and substantial genetic heterogeneity of AML, monitoring measurable residual disease (MRD) has become an effective approach to evaluate the response to chemotherapy and to predict relapse. However, the clinical implications of NGS MRD change after allogeneic hematopoietic cell transplantation (alloHCT) are still under investigation. The aims of this retrospective study are to verify whether alloHCT improved the outcome of AML patients with NGS MRD positive status in pre-transplant and to investigate how pre- and post-transplant NGS MRD status changes affect the outcome of patients with AML.
Methods: This study analyzed patients of age more than 18 years who underwent alloHCT between 2018 and 2022 at single center. NGS mutation test was obtained at diagnosis, and every 3 months after stem cell transplant for 2 years with synchronized peripheral blood chimerism tests. Requirement for inclusion in this retrospective cohort study was availability of NGS mutation results at pre-transplant and at 3 months, as well as donor chimerism results after alloHCT. Patients with no mutations by NGS at diagnosis and at pre-transplant were excluded.
Patients were classified by the NGS MRD status in pre-transplant and at 3 months post-transplant: Positive MRD to Positive MRD (Group A), Positive MRD to Negative MRD (Group B), Negative MRD to Positive MRD (Group C), and Negative MRD to Negative MRD (Group D). Patient characteristics are in Table 1.
The Kaplan-Meier method and log-rank tests were used to estimate the survival and to compare the differences in survival. Statistical analyses were performed with GraphPad Prism version 9.1.0 (Prism Inc), Microsoft Excel (Microsoft Corporation).
Results: Median follow-up was 21 months (range, 3-66). One hundred sixty-five patients met inclusion criteria. Among these, 104 (63.0%) were MRD positive, and 61 (37.0%) were MRD negative by NGS at pre-alloHCT. Fifty-one of the MRD positive patients (49%) became MRD negative by NGS at 3 months after alloHCT. The conversion rate to MRD negative from positive by NGS was not different by conditioning regimen (myeloablative (MA) 54.3% versus reduced intensity (RIC) 49.2%, p=0.67), or by AML risk group (intermediate 48.9% versus adverse 44.7%, p=0.84).
Four years cumulative incidence of relapse (CIR) of each group was statistically different between Group A and the others (Group A 47.3%, Group B 17.7%, Group C 25.9%, and Group D 10.9%, $p<0.001$), but not different between Group B, C and D ($p>0.5$). Median OS was 17 months for Group A, 27 months for Group C, but the other groups did not reach. Four-year OS of each group was statistically different between Group A, Group B, and Group D (Group A 21.1% (95% CI: 2.0 - 53.8), Group B 55.2% (95% CI: 38.7 - 68.9), Group C 50.0% (95% CI: 20.8 - 73.6), and Group D 79.3% (95% CI: 63.7 - 94.9), respectively, $p< 0.05$). Among 12 patients who were MRD positive by NGS in post-alloHCT, but not in pre-alloHCT (Group C), 3 had clinical relapse, at 4 months, 6 months, and 26 months, respectively. Five patients had NGS mutations different from the initial diagnosis. They did not show clinical relapse and maintained 100% peripheral blood lymphoid (CD3) donor chimerism throughout the observation.
Conclusion: This study showed alloHCT could convert 49% of pre-transplant MRD positive patients to MRD negative by NGS. However, there were no differences in conversion rate by intensity of conditioning regimen or by AML risk group. Combining pre- and 3 months post-transplant MRD status by NGS could discriminate prognostic subgroups in post-transplant MRD positive and negative group each and may be useful in designing post-alloHCT therapies.

Disclosures Suh: *Kite Pharma:* Membership on an entity's Board of Directors or advisory committees. **McKiernan:** *Sanofi:* Speakers Bureau.

Table 1. Characteristics of Patients by NGS MRD status in pre- and 3 months after alloHCT

	Group A NGS MRD + to +	Group B NGS MRD + to -	Group C NGS MRD - to +	Group D NGS MRD - to -	Entire Cohort
Number of patients	53	51	12	49	165
Median Age (range)	62 (23-77)	61 (26-78)	60 (33-76)	51 (21-69)	58 (21-78)
Patient Sex (M:F)	30:23	31:20	9:3	25:24	95:70
Conditioning regimen					
MA	16	19	5	21	61
RIC	31	30	5	25	91
NMA	6	2	2	3	13
Stem cell source					
BM	7	11	4	17	39
PBMC	46	40	8	32	126
Donor type					
Haplo	18	11	5	13	47
MMUD	3	5	0	5	13
MUD	26	29	5	20	80
RMD	6	6	2	11	25
AML risk group					
favorable	3	7	1	4	15
intermediate	24	23	9	23	79
adverse	26	21	2	22	71

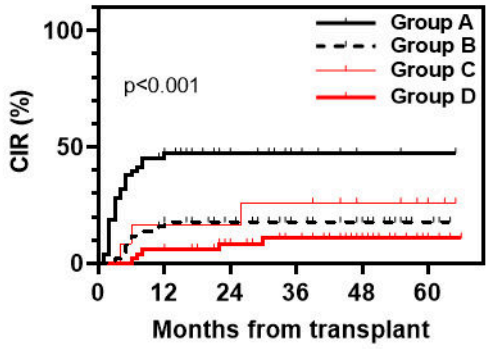

Figure 1. Comparison of Cumulative Incidence of Relapse (CIR) between groups by NGS MRD status changes pre- and 3 months after alloHCT

Figure 1

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